CLINICAL PROCEEDINGS

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VOLUME IX NUMBER 9

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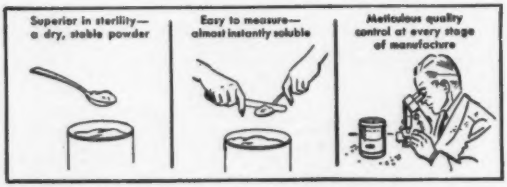

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CLINICAL PROCEEDINGS

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CONGENITAL MEGACOLON

A Review

Theodore H. I. Chuang, M.D.

INTRODUCTION

The term megacolon may be applied to any abnormal massive enlargement of the entire colon or one of its parts. While there were reports on "idiopathic dilatation of the colon" over a hundred years ago, it was Hirschsprung[1] in 1888 who first reported two cases of megacolon with the postmortem findings of massive dilatation and hypertrophy of the muscular wall, inflammation and ulceration of the mucosa, and abscess formation in the submucosa of the diseased colon. Both of his cases gave a history of obstinate constipation shortly after birth and therefore the disease was thought to be congenital in origin. As there was no demonstrable obstruction between the upper dilated colon and the lower empty rectum, Hirschsprung attributed the cause of the disease to a congenital dilatation of the colon, and thus he unwittingly implanted a misconception which persisted in the minds of later observers for almost half a century.

In the ignorance of the real cause of the disease, numerous theories were advanced and various operations were attempted with uncertain results. Advocates of lumbar sympathectomy believed that the disease was due to an over-activity of the sympathetic nerve supply to the colon[2]. Advocates of resection of the dilated part of the colon or the entire colon apparently believed in Hirschsprung's original view that the cause of the disease lay in the dilated colon[3, 4]. Finally, in 1948 after colonic motility studies with multiple-ballon technique Swenson[5, 6, 7, 8] demonstrated that the disease was due to a neurologic deficiency in the undilated rectosigmoid, interfering with the normal propagation of peristalsis. Current surgical procedures are based upon this concept. Actually, Sir Treves[9] of London, shortly after Hirschsprung's original report, had noticed the complete relief of symptoms by colostomy in "idiopathic dilatation of the colon." He performed a perineal colostomy with good result on a five-year-old girl who presented the classical picture of Hirschsprung's disease. As a wet perineal colostomy was not well accepted at this time, the beneficence of colostomy in the treatment of this malady was forgotten with it!

CLASSIFICATION AND ETIOLOGY OF MEGACOLON

It is common knowledge to the medical profession that dilatation and hypertrophy are the natural response of any hollow organ to chronic partial obstruction. The colon is not an exception. In the present state of our

knowledge, indeed, there is no justification to use the term "idiopathic" to describe any type of megacolon. On the other hand, it is essential to recognize that some type of obstruction, mechanical or functional, must be present and responsible for the clinical manifestation of megacolon. Our task is to seek and correct this obstruction.

It remains to be explained why, following chronic partial obstruction, the colon of a child seems to undergo dilatation and hypertrophy much more rapidly and extensively than that of an adult. The same phenomenon has been observed by Fawcett[10] in puppies as compared with adult mongrel dogs. Whatever the explanation may be, this fact is certainly one of the reasons why the subject of megacolon is much more frequently encountered in pediatric literature. By virtue of this same fact, it is conceivable that relatively benign obstruction to the bowel such as simple constipation due to fecal impaction, may readily result in pathological enlargement of the colon of a child and especially that of an infant.

Recognizing that megacolon, especially in children, is only a manifestation on the part of colon following some sort of obstruction, the classification of the disease is most logically put in the following way[11]:

1. Megacolon with grossly visible organic obstruction: This group includes those cases with enlarged colons resulting from either congenital or acquired lesions, such as imperforate anus with perineal or rectovaginal fistula, stricture of the rectum, or an intrinsic or extrinsic tumor reducing the size of the bowel lumen. Patients with these defects may frequently develop such massive fecal accumulation and impaction that a preliminary colostomy becomes mandatory before the definitive surgical correction of the primary lesions.

2. Megacolon without grossly visible organic obstruction: Due to the lack of visible obstruction, this group has been the source of much confusion in the literature. On a working basis it is perhaps best to subdivide this group of cases into two types as follows:

(a) Congenital megacolon: this may adequately be called aganglionic megacolon. The term "Hirschsprung's disease" should either be discarded or limited to this type of case. Aganglionic megacolon is caused by a functional obstruction at the rectosigmoid region due to a congenital absence or scarcity of the ganglionic cells of the myenteric plexus. The latter results in an abnormal or disorganized peristalsis as readily shown by multiple-balloon technique or occasionally under fluoroscopic examination with barium enema.

(b) Functional megacolon: this is described by some authors[12, 13] as "idiopathic" because there is more uncertainty as to the cause of the disorder. Lee and Bebb[14] have objected to the term "idiopathic". According to these authors, the cause of obstruction is usually fecal impaction result-

ing from faulty bowel care. Fecal impaction, spasticity of the anal sphincter with or without fissure in anus, and painful defecation seem to form a vicious cycle. This cycle may also be initiated by improper diet or formula. Redundant sigmoid (dolichocolon of Martinotti) has been incriminated by Lee and Bebb as another cause of fecal impaction due to over absorption of water from feces by the excessively long organ. Ratvitch[14] believes that such a redundant colon may actually cause obstruction by a kink or chronic partial volvulus.

PATHOLOGY OF CONGENITAL MEGACOLON

It is the present general belief that the functional obstruction at the rectosigmoid region in congenital megacolon is due to the absence of ganglionic cells of the myenteric plexus. However, the reported studies on the myenteric plexus in this disease have not been many and uniform. Whitehouse and Kernohan[15] summarized the literature on this subject recently and found only nine reports, including a total of eighteen cases, since Tittel's first report in 1901. They added eleven cases studied by them and concluded that, in congenital megacolon, the ganglionic cells were absent from the narrowed rectosigmoid down to the anal sphincter and that this pathology often extended for a variable distance proximally in the dilated colon.

The wide experience of Swenson on this subject has confirmed such observations. There can be little doubt that this anatomical deficiency in nerve structures is responsible for the loss of the colon's capacity for propulsive peristalsis by intramural reflexes. However, Ravitch[16] has expressed his doubt of the absence of ganglionic cells in a certain number of cases of congenital megacolon. This controversy may probably be solved by considering the following two points:

In the first place, variations from the usual pathological pattern of the disease have been reported although the incidence of these variations cannot be ascertained at present. The variation may be a megacolon and megarectum with the absence of ganglionic cells only in the most distal portion of the rectum[11, 17] or it may be a segmental absence of ganglionic cells for only a few centimeters of bowel wall[18]. In these cases, the aganglionic portion of the bowel may not be discovered due to unavailability of the specimen in the first instance or due to lack of studies by serial section in the second.

In the second place, there have been few studies done on the correlation between physiological and histopathological findings in this disease. Although the correlation between abnormal colonic motility and absence of the ganglionic cells seems to be logical and well demonstrated, the possibility of abnormal colonic motility without the absence of ganglionic cells

has not been thoroughly investigated. It is well known that an organ may have abnormal function without demonstrable histological abnormalities. Until we have done more colonic motility studies in cases of the so-called functional or "idiopathic" megacolon, a definite conclusion can not be drawn.

FIG. 1. An area of spasm is to be noted at the terminal portion of the rectum. This is a consistent finding in Hirschsprung's disease.

CLINICAL PICTURE

The classical clinical picture of a full-blown case of congenital megacolon is well known. However, there are a few points which deserve special remarks. The history of bowel difficulties in congenital megacolon usually dates back to the first few weeks of life. Over a period of a few months or years, the colon becomes progressively distended with feces and gas, leading to marked abdominal distension, malnutrition, and even cardiorespiratory distress. It is usually at this stage when one first suspects the presence of

this disease. Sometimes, however, a severe case may come to medical attention shortly after birth as a case of acute intestinal obstruction without ever having a bowel movement. The clinician may thus be easily misled to the diagnosis of intestinal atresia. At other times, a mild case may escape the early detection of symptoms and the diagnosis of megacolon may be made by means of barium enema studies done on a constipated but otherwise normally developed child.

The higher incidence of the disease in the male than in female (nine to one) is not explained. A difference between the male and female in the developmental anatomy of pelvic viscera may have a bearing on the interruption of parasympathetic nerve supply to the part of colon in question. The frequent presence of hypotonia of the urinary bladder in this disease must be recognized. In Swenson's series of twenty patients studied with cystometrograms, all but one showed this defect. This bladder hypotonia, besides suggesting a possible common etiological factor between the bladder and rectosigmoid pathology, indicates that a through urological study should be made in every case of congenital megacolon in order to effect adequate preoperative and postoperative care.

Congenital megacolon can usually be differentiated from functional megacolon by its history of early onset of bowel difficulties, by the finding of an empty rectum on digital examination, by its more deteriorating clinical course, and finally, by a carefully conducted barium enema study of the large bowel. Swenson and Neuhauser[6, 5], have repeatedly emphasized the importance of demonstrating the narrowed rectosigmoid by the slow administration of a small amount of barium and fluoroscopic observation in the oblique view. It must be made clear, however, that this narrowed rectosigmoid is not completely functionless, and, though working abnormally, it can constrict and particularly can dilate[19].

SURGICAL TREATMENT OF CONGENITAL MEGACOLON

Although the indications for surgical treatment of congenital megacolon have not been unanimously agreed upon, the tendency apparently is to employ some form of surgery when the diagnosis is established. Such action is certainly justified if one considers that true congenital megacolon often kills a child by severe malnutrition, cardiorespiratory complications, acute intestinal obstruction, and intestinal perforation, and that present-day surgery for megacolon is attended by low mortality and morbidity. Mild cases of congenital megacolon, however, should certainly be given a period of trial with medical treatment. While Swenson advocates surgery on most of the patients so diagnosed, Grimson[19] claims that, after a few years of medical treatment, most of his cases have had regular bowel movements in later life.

The surgical procedures designated before the recognition of fundamental pathology in congenital megacolon were largely of two types, sympathectomy and resection of the dilated part of colon or the entire colon[3, 4, 20, 21]. Judd and Dixon[20] reported 23 patients who had some type of sympathectomy for megacolon; only one obtained good results, 8 obtained fair results but still required enemas and laxatives; 14 showed no improvement. The same authors reported on the results of resection of varying amounts of colon; 36 out of 43 cases of such surgery produced good results, six additional patients showing improvement of their condition. Although the results of colectomy are certainly much better than those of sympathectomy, this procedure as compared with rectosigmoidal resection leaves much to desire and is physiologically unsound. Lee and Bebb[14] believe that the apparent results obtained from colectomy are due to the following reasons: (a) There is a lack of workable basis to differentiate congenital megacolon from functional megacolon; (b) Some benefit may be due to preoperative enemas and prolonged medical treatment; (c) Resection of a long segment of bowel not only removes the existing fecal impaction, but also renders the feces more liquid and thus delays the formation of new fecal impaction; (d) Cases have not been followed long enough for recurrences.

The present day surgery for congenital megacolon can either be emergency or elective in nature. Emergency surgery may become necessary, in the first place, for acute intestinal obstruction. This complication can usually be relieved by removal of fecal impaction by oil retention enema, high irrigation, and manual removal through the anus. Occasionally, however, fecal impaction can be successfully removed only with the help of a colostomy; this is especially true after the injudicious use of a large amount of barium during roentgenological examination. Colostomy is also indicated in poor risk patients with severe malnutrition[20].

Two things must be remembered in doing a colostomy: first, the colostomy must be made at such a site as not to interfere with the mobilization of the colon during subsequent rectosigmoidal resection; and, secondly the decision concerning the need for doing subsequent surgery must be made before doing the colostomy, because once the colostomy is made, there may not be chance again to make a certain diagnosis of congenital megacolon by means of barium enema. Intestinal perforation is the second indication for emergency surgical intervention. The site of perforation is usually at the distal part of the dilated colon. Exteriorization of the perforated bowel to form a colostomy in the left lower quadrant of the abdomen is probably the surgical procedure of choice, because the perforated bowel wall is usually markedly inflamed and is unsuitable for closure of perforation. If, however, the site of perforation, and therefore, the site of colostomy, may in-

terfere with future definitive surgery, closure of the perforation, local drainage, and a proximal colostomy should be the alternative procedure.

In contemplating elective surgery for those cases with failure of medical treatment, it goes without saying that an adequate preparation of the large bowel by evacuation of fecal impaction and bowel sterilization by chemotherapy or antibiotics is essential. Hiatt[17] reports that 60 per cent of 42 cases gave a history of extreme weakness, anorexia, and sweating for a variable period of time following tap water enemata. Three patients were in shock-like states. This author maintains that this post-enema crisis is due to water intoxication following the diffusion of a large amount of water through the huge bowel into the circulation and it is made worse by the use of prostigmine or mecholyl because of the increased hydrostatic pressure in the colon. He recommends the use of normal saline or 7 per cent gelatin solution for enemata.

The definitive surgical procedures for treating congenital megacolon that deserve mention today are (a) abdominoperineal resection of the rectosigmoid and rectum of the pull-through type with the preservation of the anal sphincter[8], (b) trans-abdominal anterior resection of the rectosigmoid and resection of the dilated colon with preservation of the rectum[21], and (c) the Correa Netto's operation[22, 23].

Of State's fifteen cases treated by trans-abdominal resection of the rectosigmoid and the dilated colon with end-end anastomosis just below the pelvic floor, fourteen were relieved and one was improved. There was no death in this series[21]. Of the seventy cases of abdominoperineal resections performed by Swenson[8], 60 patients were completely relieved and 8 patients still require occasional enemas. There were two deaths in this series. The difference in the results of these two operative procedures is statistically insignificant. The abdominoperineal operation should theoretically result in a higher percentage of cures because of a more adequate resection of the aganglionic segment of bowel. On the other hand, Swenson himself has emphasized that in doing the abdominoperineal operation for congenital megacolon, the dissection in the pelvis should be kept as close to the rectum as possible in order to avoid damage to the nervi erigentes; the danger of future impotence in these children as a complication of the operation is real.

Based upon the concept that the disorder is an achalasia of one or more functional sphincters of the rectosigmoid, especially the pelvirectal sphincter, Correa Netto has performed myotomy of these sphincters, as in Heller's procedure for cardiospasm and megaesophagus[22, 23]. The results of the surgery seem to be good in his hands. Other authorities on congenital megacolon seem to have no experience with this operation at present. If further studies made along this line should prove this operation valuable,

pelvirectal sphincterotomy will be the operation of choice for congenital megacolon because it may avoid the complications of rectosigmoidal resection, namely, sexual impotence, disturbance of bladder control, stricture at the level of anastomosis, and presacral space infection with or without a leak at the anastomotic line.

SUMMARY

1. Megacolon has been described as not due to a mysterious dilatation of the large bowel but the natural response of a hollow organ to chronic partial obstruction.

2. The logical etiological classification of megacolon has been discussed.

3. Although congenital megacolon is believed to be due to an absence of ganglionic cells of the myenteric plexus in the rectosigmoid area, and the resultant functional obstruction at that region due to disorganized peristalsis, it is suggested that more physiological studies on bowel peristalsis should be undertaken to rule out the possible existence of abnormal peristalsis without histological abnormalities in some cases of the functional megacolon.

4. Certain clinical features of congenital megacolon are discussed.

5. Various surgical procedures for treatment of congenital megacolon and their relative merits have been discussed.

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HERPES ZOSTER AND VARICELLA SIMULATING POLIOMYELITIS

Case Report No. 272

Stanley I. Wolf, M.D.*
Discussed by Robert H. Parrott, M.D.

This five-year-old white girl was well until the day prior to admission to the hospital when she began to complain of pain in her left thigh. This symptom was partially relieved by bed rest and hot moist applications to the area. The child said she felt cold; her mother did not take her temperature. During the night the pain awakened the patient but was somewhat relieved following the administration of aspirin. On the morning of admission there was severe aching pain in the left ankle. When the child refused to bear weight on her left leg she was taken to the Naval Dispensary and from there referred to The Children's Hospital as a possible poliomyelitis case. There was no vomiting, headache, or pain in other areas of the body.

The patient had been exposed to chickenpox in the neighborhood about nine weeks before admission. No more recent exposure was known to the mother. Ten days before admission the patient developed a rash which was diagnosed as poison ivy by a local physician. This had virtually healed except for scattered crusted areas on the body at the time of admission. There was no history of recent inoculation or injection. Both parents and three siblings were all living and well. None of them had vesicular lesions in any area of the body.

Physical examination on admission revealed a crying, rather uncooperative, apprehensive, alert five-year-old girl who did not appear acutely ill. Her temperature (rectal) was 100.0 degrees F. Her neck was supple. She complained of severe pain in the left thigh and resisted all movements of this part. There was no redness, swelling or point tenderness in this area. She also complained of pain in her left ankle, but movement of the foot was not resisted nearly so much as movement of the thigh. The right lower extremity was normal. Reflexes were normal except for a diminished patellar reflex on the left. No muscle weakness was noted.

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On the face, anterior trunk, and left upper posterior thigh were noted occasional dry, slightly crusted, old skin lesions which were thought to be due to the former contact dermatitis described. No vesicular eruption was noted anywhere on the body at the time of admission.

Lumbar puncture on admission revealed a clear cerebrospinal fluid with 15 white blood cells, 94 per cent lymphocytes, 6 per cent polymorphonuclear leukocytes. The protein was 15 mgm. per cent and sugar 48 mgm. per cent. Complete blood count and urinanalysis were normal. The corrected sedimentation rate (Wintrobe) on admission was 18 mm/hour. The child was placed on absolute bed rest and observed as a possible case of poliomyelitis.

On the second hospital day a vesicular eruption was noted involving the left postero-medial thigh, lower buttock and labia majora. These vesicles were closely grouped on a non-erythematous base and were about 2–3 mm. in diameter. They appeared first in the areas previously thought to be affected with poison ivy, but soon spread to adjacent areas.

When more lesions appeared the next day, the diagnosis of herpes zoster was entertained. On the second hospital day the patient's temperature became 101.0 degrees (F) and on the next day, after a brief return to normal, the temperature spiked to 104.2 degrees and a new vesicular eruption was noted on her trunk. The diagnosis of varicella was made and repeat lumbar puncture was ordered. The cerebrospinal fluid at this time was clear and showed 23 cells, 70 per cent polymorphonuclear leukocytes, 30 per cent lymphocytes, 37 mgm. per cent of sugar and 35 mgm. per cent protein. There were no clinical signs of encephalitis.

On the fourth hospital day no new lesions were noted and those already present seemed to be healing with the use of Burrow's solution soaks and calamine lotion. The patient's temperature was now 101.0 degrees (F). She was able to move her left thigh freely in all directions with no discomfort. The next day the patient was afebrile and able to walk satisfactorily. Her skin lesions were crusted. She was sent home on bed rest.

Two weeks later the patient was seen at the Naval Dispensary. She had completely recovered, had no pain or weakness and walked well. The lesions on the body and left thigh had almost completely healed. The doctors at the dispensary were impressed with the resemblance of the healing lesions to herpes zoster. She had apparently done well up to the present time.

DISCUSSION

One can only speculate concerning the etiology of the fever and vesicular lesions in this little girl, but her case serves well to initiate a review of the similarities and differences between varicella and herpes zoster and the possibility of the co-existence of these two diseases in a single host.

Of course this case also must be added to the large list of conditions to be considered in the differential diagnosis of poliomyelitis.

Did the child clinically have herpes zoster? Pain and tenderness preceding a vesicular skin eruption over what may well have been a segmental distribution of sensory nerve roots favors this diagnosis strongly. The mild cerebrospinal fluid lymphocytosis present at this time often occurs in patients with herpes zoster. Since the vesicles first appeared in the sites of a dermatitis which occurred 10 days previously, one might wonder if the

former lesions had also been due to herpes zoster (lesions often appear sporadically for several weeks) or whether they provided a site of entry for herpes zoster (incubation period of 7–14 days is consistent).

Did the child have varicella? There was varicella in her neighborhood even though she had no established contact with a case since nine weeks before admission. She had high fever and a vesicular eruption which covered her trunk, persisted for three days, and then became crusted, features which are consistent with a varicella diagnosis. On the other hand, the skin lesions were not described as being pruritic nor as occurring in successive crops with lesions in various phases, features which tend to negate the chicken-pox diagnosis. It is also true that aberrant vesicles of herpes zoster may be so numerous as to simulate varicella.

Concomitant occurrence of herpes zoster and varicella in this child is consistent with former reports and is a very attractive hypothesis, especially in consideration of the similarity between the viruses which cause these two illnesses. The micro-organisms are very similar in size and electron-microscope appearance. In humans herpes zoster virus has induced apparent varicella and varicella contact has initiated herpes zoster. The vesicular skin lesions and the intranuclear inclusion bodies found in the lesions of each of these diseases are similar. Available evidence indicates, however, that there is no cross immunity between the two. A summary of some of the clinical and epidemiological differences between herpes zoster and varicella is presented in the accompanying table.

Clinical and Epidemiological Differences Between Varicella and Herpes Zoster

	HERPES ZOSTER	VARICELLA
Incubation period	7–14 days	14–16 days
Greatest age incidence	>20 years	<20 years
Sex incidence	M > F	Equal
Communicability	Low	High
Occurrence	Sporadic	Epidemic
Distribution of lesions	Segmental	Trunk Oropharynx Extremities
Sensory symptoms	Pain	Pruritis
CSF involvement	Usual	Unusual

Perhaps the reason that there is no convincing explanation for the somewhat contradictory relationship between herpes zoster and varicella is that there has previously been no consistently reproducible laboratory method for the isolation of these viruses. The recent isolation of varicella virus by tissue culture methods offers good promise of supplying the tools with which to carve out the answers to some of these questions in the near future.

HEAT PROSTRATION IN MUCOVISCIDOSIS

Case Report No. 273

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INTRODUCTION

This case report illustrates the recently recorded observation that patients with mucoviscidosis are especially susceptible to heat prostration during prolonged periods of high atmospheric temperatures.

CASE PRESENTATION

A two-and-a-half year old white female was admitted to The Children's Hospital on April 25, 1952, with the chief complaint of chronic cough of 18 months duration.

The history revealed that she apparently was well until 18 months prior to admission when she developed a cough which became progressively worse. The cough was non-productive in nature. Fetor oris was present and the appetite was poor.

The past history revealed that the patient was the product of a full term pregnancy and an uneventful delivery. Her birth weight was 5 pounds 7 ounces. She had a normal development. The family history revealed that the father and mother were living and well, and one sibling, three and one-half years old, was in good health.

Physical examination revealed a temperature of 98.0 degrees F., pulse rate of 120/min., and respirations of 50/minute. The child was a well-developed and well-nourished white female who coughed frequently. A mild erythema on the flexor surface of the left arm was noted. Her throat and ears were injected. The rest of the examination was normal.

The laboratory examinations revealed a normal urine and hemogram. A roentgenogram of the chest showed a shadow in the medial half of the left chest extending from the third interspace anteriorly near the mediastinum. A bronchogram revealed a large one and one-half by one and one-half inch space in the medial aspect of the left lower lobe filled with lipiodol, with a moderate degree of bronchiectasis in this region and a very early degree of bronchiectasis in the right lower lobe. The possibility of lung cyst or abscess of the left lower lobe was suggested. A left thorocotomy was performed on May 1, 1952, which revealed a firm mass in the left lower lobe, and a left lower lobectomy was performed. The post-operative course was satisfactory and the child was discharged 8 days later.

The patient was well until July 23, 1952, when, during a severe heat wave in Washington, D. C., she began vomiting. She was admitted to The Children's Hospital. Her temperature was 103°, the pulse very weak (144/min.) and respirations 100/min. and Cheyne-Stokes in type. The tissue turgor was very poor. The hands, lips, and feet were cyanotic. The throat was injected and wheezing rales were audible at the left base. The liver was one finger breadth below the costal margin. The CO_2 combining power on admission was 19 volumes per cent. In spite of oxygen and parenteral fluids, her condition worsened. She developed a generalized convulsion and expired shortly thereafter.

An autopsy was performed and the findings were bronchiectasis, pleural adhesion on the left, and broncho-pneumonia. Microscopically the pancreas showed an atrophy of the acinar tissue with a relative increase in the fibrous connective tissue; the lobules were separated by fat cells. The impression was mucoviscidosis.

DISCUSSION

Since 1905, when Landsteiner[1] recorded the earliest pathological description of the pancreatic lesion in mucoviscidosis, to the present a wealth of medical experience has accumulated which serves to crystallize the physiologic alterations produced by this disease entity. Until Farber[2] demonstrated the systemic nature of the disease and suggested the term "mucoviscidosis", the pathology was thought to be limited to the pancreas. It is now evident that the same basic defect is responsible for the respiratory complications. Indeed, Shwachman[3] has indicated that the duodenal juice of some patients with mucoviscidosis may have a normal tryptic activity. In such instances, chronic respiratory disease with little or no gastro-intestinal symptoms will be the presenting feature. Undiagnosed during life, our patient would seem to fall into this category. As experience has broadened our knowledge, it has become evident that this disease is a disturbance of many glandular tissues.

Most recently, Kessler and Andersen[4] recorded an abnormally high incidence of heat prostration in children with mucoviscidosis. Of 12 children seen during periods of high atmospheric temperatures who presented a similar clinical picture, seven had a diagnosis of mucoviscidosis. The heat prostration was manifested by a sudden onset, after approximately 48 hours of hot weather, of marked dehydration, fever, and signs of circulatory collapse in the absence of any obvious clinical evidence of acute infection. Most of these patients were perspiring freely on admission. Among the laboratory data on their patients, the two serum chloride values reported are both markedly lowered. It is of interest that one of these children was considered a well child and his pancreatic deficiency was not discovered until a subsequent admission. In our case the heat prostration resulted in the death of the patient and the unsuspected diagnosis of mucoviscidosis was made only after autopsy.

It remained for Darling and his co-workers[5] to offer a reasonable explanation of the susceptibility to heat casualty which these patients show. In a unique, controlled experiment, they demonstrated that the chloride concentration of the sweat in patients with mucoviscidosis was more than three-times that in control subjects. When measured, the sodium was somewhat higher than the chloride. It is shown that these patients have normal renal mechanisms of salt retention, that the gastro-intestinal tract is not the avenue of excessive salt loss, and that no primary adrenal dysfunction is present. By exclusion, the cause of the excessive salt loss in the sweat probably lies in the abnormality in this disease. The primary mechanism which renders patients with mucoviscidosis especially susceptible to heat prostration lies in excessive salt loss in the sweat.

These observations have a number of practical applications:

(1) A diagnosis of mucoviscidosis should be considered in any patient who has chronic respiratory disease with or without associated gastrointestinal symptoms.

(2) Mucoviscidosis should be suspected in infants and children with heat prostration who have previously been considered healthy.

(3) During periods of high atmospheric temperatures, patients with mucoviscidosis should be placed in an extra salt and fluid intake as a prophylaxis against heat prostration.

(4) It is erroneous to recommend that patients with mucoviscidosis be moved to a warm, dry climate in an attempt to lessen exposure to respiratory disease.

SUMMARY

A case of heat prostration resulting in the death of an 18 month old white female has been presented. On autopsy an unsuspected diagnosis of mucoviscidosis was established. The probable etiology of the susceptibility of patients with mucoviscidosis to high atmospheric temperatures has been reviewed and the practical applications of these observations have been noted.

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The following are abstracts of papers which received awards for their excellence from the Committee on Publications at the annual meeting and banquet of the Children's Hospital Alumni Association, which was held at the Carlton Hotel on May 12, 1953. These awards are made annually.

CORRECTION OF ACIDOSIS WITH SODIUM SUCCINATE*

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Prior to 1932, intravenous sodium bicarbonate had been used in the treatment of acidosis. Following the work of Hartmann and others, sodium lactate has become more widely accepted in the treatment of severe bicarbonate deficits. Occasionally, however, one encounters an acidotic patient who has lost the ability to oxidise lactate. With this fact in mind, an experimental problem was devised to evaluate sodium succinate as an alkalinizing agent.

All patients for the study were selected from the diarrhea service of the Children's Hospital. Patients with carbon dioxide combining powers of less than 14 millimoles were accepted for treatment with sodium lactate or sodium succinate. In addition to carbon dioxide combining powers, the blood pH values and ionic concentrations of potassium, sodium, and chloride were determined.

The patients studied showed variations in whole blood carbon dioxide combining power from 7 to 14 millimoles, and the pH values varied from 7.00 to 7.31. The group of patients receiving sodium succinate were compared statistically to the group receiving sodium lactate. It was found that there was no significant difference in the rapidity or degree of improvement in the two groups. The potassium, sodium, and chloride values were within the normal range in all the cases and showed no unusual variation during the period that was required for the acidosis to be corrected. There were no acute or chronic toxic effects noted in any of the patients receiving the sodium succinate.

* This study was aided in part by a grant by Brewer and Co.

CLINICAL AND LABORATORY DIFFERENTIAL DIAGNOSIS BETWEEN HERPANGINA AND INFECTIOUS (HERPETIC) GINGIVOSTOMATITIS*

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The etiological relationship of herpangina to a certain group A Coxsackie viruses and of acute infectious gingivostomatitis to herpes simplex virus has been amply demonstrated. A differential diagnosis between these two diseases has also been described. The typical case of herpangina is seen in children during the summer months and is characterized by sudden onset of rather high fever with anorexia, dysphagia and sore throat. In the pharynx are noted grey-white papulo-vesicular lesions about one or two millimeters in diameter on an erythematous base which progresses to form slightly larger ulcers. These lesions are usually found on the anterior pillars, uvula, soft palate, or tonsils. The symptoms persist about two or three days; the throat lesions are in evidence for four to six days after onset of illness.

Gingivostomatitis is a common ailment seen throughout the year in children of about the same age group as herpangina. The usual case reveals the gradual onset of fever, sore mouth, dysphagia, foul breath and bleeding gums.

Physical examination reveals a rather ill child with hyperemic, hypertrophic and hemorrhagic gingivae and cervical lymphadenopathy. Vesiculation and/or ulceration throughout the mouth are common. The fever lasts 3 or 4 days; the oral lesions persist for 8 to 12 days.

Despite the difference in clinical pictures of these two diseases, many clinicians have questioned the validity of this differential diagnosis. In fact, since both viruses can cause rather similar symptoms in suckling mice, laboratory differentiation has also been a problem.

In an attempt to settle some of these questions, it was decided to undertake a concurrent study of patients with herpangina and infectious gingiviostomatitis from the clinical as well as the etiological viewpoint. The study was conducted during July, August, and September 1952 at the Children's Hospital, Washington, D. C.

All the cases in the study were diagnosed from the clinical picture and hospitalized for careful study.

Of a total of twenty-five children hospitalized for this study, thirteen

* This study was carried out in collaboration with Robert J. Huebner, M.D., Senior Surgeon and Robert H. Parrott, M.D., Senior Assistant Surgeon, Department of Health, Education and Welfare, Public Health Service, National Institutes of Health, National Microbiological Institute.

were diagnosed as having herpangina and twelve as having infectious gingivostomatitis. All had fever and discrete lesions in the mouth or pharynx. The clinical impression was based primarily on the location of the lesions with consideration of suddenness of onset, degree of fever and lymphadenopathy as previously described.

Fever was uniformly present in all cases. Anorexia and soreness in the mouth or throat were prominent symptoms in both diseases, being present in all cases of gingivostomatitis. All cases of herpangina had ulcerations on the soft palate and/or anterior pillars. In no case was bleeding or ulceration noted on the gums, buccal mucous membranes, lips, tongue or posterior pharyngeal wall.

In the gingivostomatitis series, all cases had gum involvement, either with hypertrophy or ulceration or both. Bleeding of the gums was frequently noted. Ulcerations elsewhere in the mouth, including the anterior pillars and soft palate, were common.

Of 13 herpangina patients, group A Coxsackie viruses were isolated from eleven. Of 12 gingivostomatitis patients, herpes virus was isolated from ten.

In four of the patients clinically diagnosed as having gingivostomatitis, group A Coxsackie viruses were also isolated. From three of these patients, one of whom had ulcers on the anterior pillars, both viruses were recovered. In one there was no laboratory evidence of herpes infection. This patient had not only ulceration and hyperemia of his gingivae but also ulceration of his anterior pillars. His total illness lasted five days.

Acute and convalescent sera from four of the patients with gingivostomatitis were tested for their capacity to neutralize herpes. All showed a rise in titers in their convalescent specimen.

The bacterial and fungal florae of the oropharynx in both diseases were found to be similar and consistent with the normal flora of the mouth. Total leukocyte count on the peripheral blood ranged between 5,100 and 12,800 with the great majority around 7–8,000. An increase in the number of lymphocytes over polymorphonuclear leukocytes was frequently noted in both diseases when counts were checked on consecutive days. The initial differential count was not significant in either disease.

The heterophile agglutination test was negative on all admissions and was also negative on the convalescent serum from the nine patients whose repeat blood was tested. No significant differences were noted in the pH of the mouth.

DISCUSSION AND CONCLUSIONS

It would appear from these studies that it is possible with fair certainty to differentiate clinically between herpangina and infectious gingivostomatitis. The location of the lesions is probably the most accurate

differential point. The presence of ulcerations or bleeding on the gums, lips, tongue or buccal mucous membranes probably rules out herpangina. Since anterior pillar lesions occur in gingivostomatitis, the mouth must be searched before the diagnosis of herpangina is made.

The laboratory data in these studies reveal the absence of other etiological factors in either of these diseases.

These studies have several practical applications; with regard to prognosis, herpangina, while sudden in onset, is a milder illness, shorter in duration and much less debilitating; and with regard to management, herpangina requires little other than aspirin and reassurance in its treatment, but gingivostomatitis patients may require local antisepsis, analgesia, hemostasis and occasionally, parenteral fluid therapy.

Antibiotics have been of no value in the treatment of either disease.

THE TOTAL CIRCULATING EOSINOPHILE COUNT UNDER ENVIRONMENTAL AND STRESS STIMULI

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Since Selye's description in 1946 of the "alarm reaction" and "general adaptation syndrome," in which eosinopenia was demonstrated to follow a stress situation, there has been a revival of medical interest concerning the function and significance of the eosinophile cell. The ACTH and epinephrine tests described by Thorn have subsquently become readily accepted as a means of evaluating the function of the pituitary-adrenal axis. Techniques of performing total eosinophile counts have been improved and normal values for adults have been established as ranging from 80 to 500 cells/cu. mm. Acute infections and traumatic procedures such as surgery have been accepted as constituting non-specific stress factors which in the normal subject produce an initial eosinopenia followed by a gradually increasing eosinophilia paralleling the recovery phase.

Relatively little work on this subject has been done in the pediatric age group. Various investigators have reported great variations in the total eosinophile count among various age groups of children. Premature newborns were found to have near-zero total eosinophile counts on the first day of life and to have counts in the range of 1000 to 1500 after one month. Total eosinophile counts in full-term newborns vary from 20 to 500 on the first day of life. Older children have counts in the normal adult range. Like adults, they, too, respond to acute infections with marked eosinopenia. The majority of newborns respond to the ACTH and epinephrine tests on

the first day of life, but in some it is delayed until the second week of life. Premature newborns have been noted to show no response to the epinephrine test until the end of the first week of life.

In the course of clinical studies on patients at Children's Hospital the authors have frequently observed marked eosinopenia occurring in the acute phase of infections and a subsequent post-toxic eosinophilia. In patients with acute pyogenic meningitis a fall in the eosinophile count during the convalescent phase was noted to presage by one or more days the recognition of a complication or relapse. It seemed important, therefore, to determine to what extent a daily total eosinophile count might vary as a result of procedures and conditions inherent in the treatment of a disease such as meningitis. If a significant variation occurred, for example, after meals and after traumatic procedures, it would invalidate the significance of the eosinophile count as a prognostic sign unless the counts were drawn under rather rigidly controlled conditions. With this in mind the present study was undertaken, using 19 patients in 3 different age groups, i.e., 11 convalescent diarrhea patients aged 2 to 12 months, 4 post-poliomyelitis patients aged 1 to 2 years and 4 post-poliomyelitis patients aged 8 to 12 years. None of the patients was receiving specific drug therapy.

Fasting eosinophile counts were within the normal adult range of 80 to 500. The oldest age group showed the least daily individual variation in fasting counts while successive counts in the 2 to 12 month age group varied widely.

There was no consistent post-prandial effect. The majority of counts, taken at 15 minute, 30 minute, and two-hour intervals, ranged within 200 cells/cu. mm. of the fasting counts.

Although there are reports in adults of a diurnal variation consisting of a mid-morning fall followed by a gradual increase to a peak in late afternoon, no consistent diurnal trend was noted in this study. Four p.m. counts ranged from 20 to 630—a wider variation than that found in fasting counts.

After intramuscular injections a consistent fall of 10 to 70 cells was found to occur in total eosinophile counts done in 15 and 30 minutes. No sustained effect was demonstrated; third counts performed two hours later were in the pre-injection range.

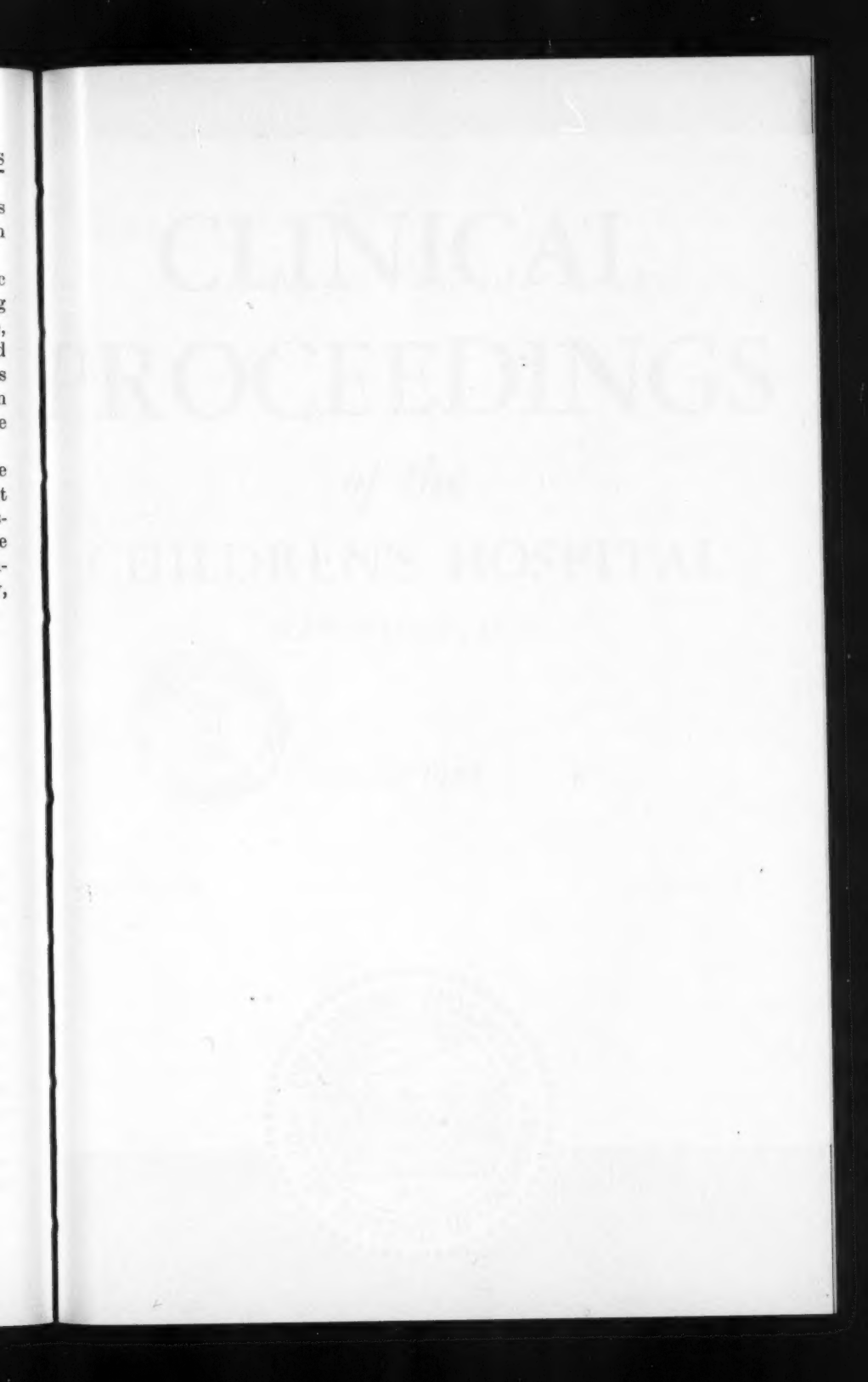
Lumbar punctures, similarly, were followed by a drop of 50 to 90 cells in eosinophile counts done 15 to 30 minutes later. Here also a return to previous levels occurred in two hours.

The eosinopenic effect of continuous, intravenous glucose administration reported by other authors was found in three patients in our study to consist of an initial fall of 30 to 40 eosinophiles in the first hour, followed by

a slow rise to the initial level in three hours. Changing the intraveonus solution to protein hydrolysate produced a second fall of 40 to 100, which gradually rose in the ensuing hours.

Other authors have reported eosinopenia in adults following therapeutic procedures (such as electroshock therapy, insulin convulsions), drug administration (including nitrogen mustards, cardiazole, sodium salicylate, vitamin C and desoxycorticosterone acetate or salt administration), and starvation and malnutrition. In addition the total eosinophile count has been found to oscillate from minute to minute, one observer reporting an extreme variation of 263 and 631 occurring in 10 counts per patient done at one and five minute intervals.

When one appreciates the wide range of stimuli which may affect the total eosinophile count, it seems remarkable that daily counts could reflect any consistent trend paralleling clinical recovery. That they do is indisputable. However, it would appear advisable to do daily eosinophile counts under as rigidly controlled conditions as possible in order to eliminate extraneous stimuli. In view of the results obtained in this study, it would appear that fasting counts are the least subject to variation.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